

What is claimed is:

1. A process for preparing crystalline desloratadine Form I comprising the steps of:
  - a) preparing a solution of desloratadine in a solvent selected from the group consisting of acetonitrile, di-methyl formamide, tetrahydrofuran and diethylcarbonate, wherein desloratadine Form I crystallizes out of the solution; and
  - b) recovering the desloratadine Form I.
2. The process of claim 1, wherein the solvent is acetonitrile.
3. The process of claim 1, wherein the solvent is di-methyl formamide.
4. The process of claim 1, wherein the solvent is tetrahydrofuran.
5. The process of claim 1, wherein the solvent is diethylcarbonate.
6. The process of claim 1, further comprising a drying step.
7. The process of claim 1, wherein the solution is cooled to about 20°C to about 30°C.
8. The process of claim 1, wherein the recovered Form I is substantially free of Form II.
9. The process of claim 8, wherein the ratio of Form II to Form I is less than about 1% by weight.
10. A process for preparing crystalline desloratadine Form I comprising the steps of:
  - a) preparing a solution of desloratadine in a solvent selected from the group consisting of chloroform and ethyl acetate;
  - b) combining the solution with an anti-solvent to precipitate desloratadine Form I; and
  - c) recovering desloratadine Form I.
11. The process of claim 10, wherein the anti-solvent is a C<sub>2</sub> to a C<sub>8</sub> ether.
12. The process of claim 11, wherein the ether is di-isopropyl ether.
13. The process of claim 12, wherein the solvent is chloroform.
14. The process of claim 13, wherein the ratio of desloratadine Form II to Form I is about 6%.
15. The process of claim 10, wherein the anti-solvent is a C<sub>5</sub> to a C<sub>12</sub> saturated hydrocarbon.
16. The process of claim 15, wherein the hydrocarbon is hexane.
17. The process of claim 16, wherein the solvent is chloroform.

18. The process of claim 17, wherein the solution has an initial temperature of at least about 40°C.
19. The process of claim 18, wherein the ratio of desloratadine Form II to Form I is about 35 to about 40% wt/wt.
- 5 20. The process of claim 17, wherein the solution has an initial temperature of less than about 40°C.
21. The process of claim 20, wherein the ratio of desloratadine Form II to Form I is about 2% wt/wt.
22. The process of claim 16, wherein the solvent is ethyl acetate.
- 10 23. The process of claim 22, wherein the ratio of desloratadine Form II to Form I is about 2% wt/wt.
24. A process for preparing crystalline desloratadine Form I comprising the step of:
- a) preparing a solution of desloratadine in a C<sub>1</sub> to C<sub>4</sub> alcohol;
  - b) combining the solution with water to precipitate desloratadine Form I; and
  - 15 c) recovering desloratadine Form I.
25. The process of claim 24, wherein the alcohol is ethanol.
26. The process of claim 24, wherein the Form I obtained has from about 2% to about 10% Form II.
27. A process for preparing crystalline desloratadine Form I comprising the steps of:
- 20 a) preparing a solution of desloratadine in isopropanol, wherein desloratadine Form I precipitates from the solution; and
- b) recovering the desloratadine Form I.
28. The process of claim 27, wherein further comprising the step of seeding with Form II to increase ratio of Form II to Form I.
- 25 29. A process for preparing crystalline desloratadine Form II comprising the steps of:
- a) melting desloratadine to obtain a molten material;
  - b) cooling the molten material to obtain a solid; and
  - c) grinding the solid.
30. A process for preparing a mixture of crystalline desloratadine Form I and Form II
- 30 comprising the step of grinding crystalline desloratadine Form I.
31. A process for preparing crystalline desloratadine Form II comprising the steps of:
- a) preparing a solution of desloratadine in dimethyl carbonate, wherein desloratadine Form II precipitates from the solution; and

- b) recovering the desloratadine.
32. The process of claim 31, wherein the desloratadine Form II recovered is substantially free of Form I.
33. A process for preparing crystalline desloratadine Form I comprising the steps of:
- 5 a) preparing a solution of desloratadine in i-butyl acetate, wherein Form I precipitates from the solution; and
- b) recovering the precipitate
34. The process of claim 33, wherein the precipitate contains from about 15% to about 25% Form II.
- 10 35. A process for preparing crystalline desloratadine Form I comprising the steps of:
- a) preparing a solution of desloratadine in a solvent selected from the group consisting of isopropanol and i-butanol, wherein desloratadine Form I precipitates from the solution; and
- b) recovering the mixture.
- 15 36. The process of claim 35, wherein the solvent is isopropanol.
37. The process of claim 36, wherein the mixture contains less than about 10% Form II compared to Form I by weight.
38. A process for preparing a mixture of crystalline Form I and Form II of desloratadine comprising the step of drying desloratadine Form I crystals obtained by
- 20 crystallization from a C<sub>1</sub> to a C<sub>4</sub> alcohol.
39. The process of claim 38, wherein the alcohol is isopropanol.
40. The process of claim 38, wherein the alcohol is isobutanol.
41. A process for making a mixture of crystalline desloratadine Form I and Form II comprising the steps of combining a solution of desloratadine in a suitable solvent with an
- 25 anti-solvent containing seeds of both Form I and Form II of desloratadine to precipitate the mixture, and recovering the mixture.
42. The process of claim 41, wherein the mixture contains from about 35% to about 65% Form I by weight.
43. The process of claim 41, wherein the solvent is iso-butyl acetate.
- 30 44. The process of claim 41, wherein the antisolvent is a C<sub>5</sub> to C<sub>12</sub> hydrocarbon.
45. The process of claim 44, wherein the hydrocarbon is heptane.
46. A process for preparing a mixture of desloratadine crystalline Forms I and II containing at least about 25% of both of the Forms comprising the steps of:

- a) preparing a solution of desloratadine in a solvent selected from the group consisting of ethyl acetate and iso-butyl acetate, in a mixture with about 3% to about 20% C<sub>1</sub> to C<sub>4</sub> alcohol by volume, wherein the mixture of Form I and II precipitates from the solution; and
- 5        b) recovering the mixture.
47. The process of claim 46, wherein the mixture contains at least about 40% of both forms by weight.
48. The process of claim 46, wherein the alcohol is present in about 10% by volume.
49. The process of claim 46, wherein the alcohol is selected from the group consisting
- 10 of methanol, iso-propyl alcohol and mixtures thereof.
50. A process for preparing a mixture of crystalline desloratadine Form I and II comprising the steps of:
- a) preparing a solution of desloratadine in iso-butyl acetate;
- b) combining the solution with a C<sub>5</sub> to C<sub>12</sub> aromatic hydrocarbon to
- 15 precipitate the mixture, wherein the combining may be carried out before, after or during crystallization; and
- c) recovering the mixture.
51. The process of claim 50, wherein the hydrocarbon is heptane.
52. The process of claim 50, wherein the mixture contains from about 60% to about
- 20 70% Form I by weight.
53. The process of claim 50, further comprising increasing ratio of Form II to Form I by seeding the solution with a mixture of Form I and Form II before crystallization.
54. The process of claim 53, wherein the seeding results in about 35% to about 45% Form I compared to Form II by weight.
- 25 55. A process for preparing a mixture of crystalline desloratadine Form I and II comprising the steps of:
- a) preparing a solution of desloratadine in iso-butyl acetate;
- b) combining the solution with iso-butyl acetate at a temperature lower than the solution to crystallize the mixture; and
- 30 c) recovering the mixture.
56. The process of claim 55, further comprising seeding the solution with a mixture of Form I and Form II before crystallization.

57. A process for preparing a mixture of crystalline desloratadine Form I and Form II comprising the steps of:

- a) preparing a solution of desloratadine in ethyl acetate;
- b) seeding the solution with a mixture of Form I and Form II;
- 5 c) combining the solution with a C<sub>5</sub> to C<sub>12</sub> saturated hydrocarbon, wherein the combining may be carried out before, after or during crystallization; and
- d) recovering the mixture of desloratadine Form I and II.

58. The process of claim 57, wherein the hydrocarbon is heptane.

59. The process of claim 57, wherein the mixture is about a 4:1 to about a 1:3 mixture  
10 of Form I to Form II wt/wt.

60. A process for preparing a mixture of crystalline desloratadine Form I and Form II comprising the steps of:

- a) preparing a solution of desloratadine in 2-propanol and toluene, wherein the mixture of Forms I and II precipitates from the solution; and
- 15 b) recovering the mixture.

61. The process of claim 60, wherein precipitation occurs as a result of cooling the solution.

62. The process of claim 60, wherein ratio of 2-propanol to toluene is less than about 20% by volume.

20 63. The process of claim 60, wherein precipitation occurs as a result of adding a C<sub>5</sub> to C<sub>12</sub> saturated hydrocarbon as an anti-solvent.

64. The process of claim 63, wherein the anti-solvent is n-heptane or n-hexane.

65. The process of claim 63, further comprising the step of seeding the solution.

66. A process for preparing a mixture of Form I and Form II, comprising the steps of:

- 25 a) providing a first solution of desloratadine in toluene;
- b) evaporating the toluene to obtain a residue;
- c) dissolving the residue in a mixture of toluene and a C<sub>1</sub> to C<sub>4</sub> alcohol to obtain a second solution;
- d) cooling the second solution to obtain a slurry;
- 30 e) combining the slurry with a C<sub>5</sub> to C<sub>12</sub> saturated hydrocarbon to precipitate the mixture; and
- f) recovering the mixture.

67. The process of claim 66, wherein the alcohol is 2-propanol.

68. A process for preparing a mixture of desloratadine Form I and Form II comprising the steps of:

a) combining desloratadine acetate, toluene and KOH to obtain a reaction mixture;

5 b) heating the mixture, whereby two phases are obtained;

c) separating the phases;

d) concentrating the separated organic phase;

e) dissolving the obtained concentrate in a toluene-2-propanol mixture containing less than about 20% 2-propanol by volume;

10 f) cooling the solution to obtain a slurry;

g) combining the slurry with cold n-heptane; and

h) recovering mixture of desloratadine forms I and II.

69. The stable mixture of claim 68, wherein the process further comprises washing the product of step c with water.

15 70. The stable mixture of claim 68, wherein the process further comprises warming the product of step f to 45°C.

71. The process of claim 68, wherein the mixture is about a 24 to about a 40% Form II compared to Form I.

20 72. A process for preparing crystalline desloratadine Form II comprising the steps of crystallizing desloratadine from toluene, and recovering the crystalline form.

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